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With international search report.

(54) Title: METHOD OF TREATMENT AND PHARMACEUTICAL COMPOSION

(57) Abstract

A method of treating asthma, allergy and inflammation comprises treatment with a leukotriene inhibitor and loratadine either concurrently in separate doses or combined in a single pharmaceutical formulation.

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CROSS REFERENCE TO RELATED APPLICATION

This application is based on, and claims priority from, provisional application number 60/011,328 filed February 8, 1996.

TITLE OF THE INVENTION

METHOD OF TREATMENT AND PHARMACEUTICAL COMPOSITION

BACKGROUND OF THE INVENTION

Loratadine is an antihistamine with H-receptor antagonist properties useful in the treatment of allergies and is described in U.S. Patent 4,282,233.

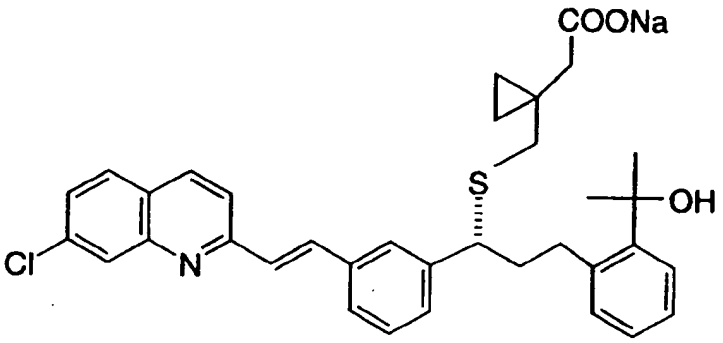
Leukotriene antagonists are known to be useful in the treatment of asthma, allergic reactions, and inflammation.

Now with the present invention, there is provided a method of treating asthma, allergy and inflammation with a combination of these two agents which is more efficacious than either agent by itself.

SUMMARY OF THE INVENTION

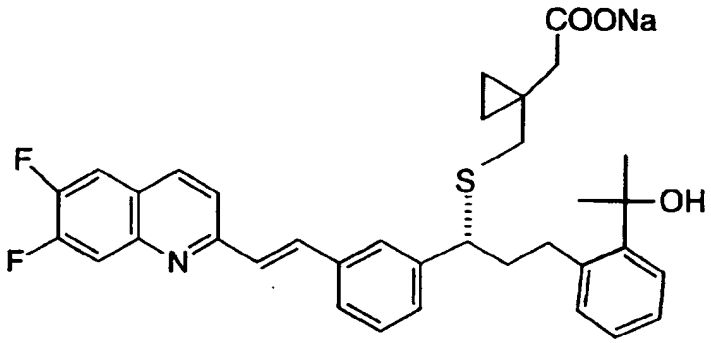
This invention is concerned with a method of treatment of asthma, allergy and inflammation by administration of an effective amount of loratadine and an effective amount of a leukotriene antagonist either by essentially concurrent administration or combined in a single pharmaceutical composition wherein the leukotriene antagonist is selected from:

A. Sodium 1-(((R)-(3-(2-(7-chloro-2-quinolinyl)ethenyl)phenyl)-3-(2-(2-hydroxy-2-propyl)phenyl)thio)methyl)cyclopropaneacetate, EP 480,717

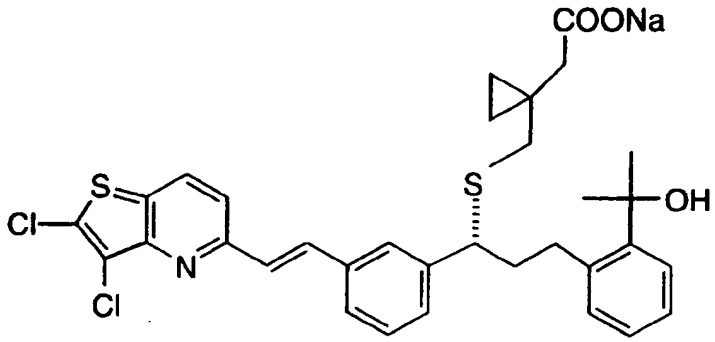


Montelukast Sodium

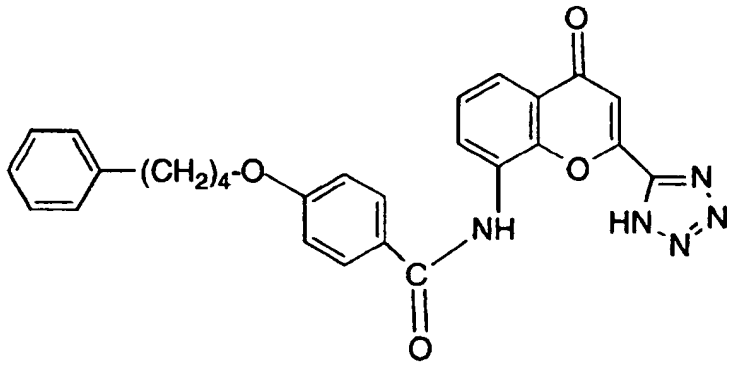
B. Sodium 1-(((R)-(3-(2-(6,7-difluoro-2-quinolinyl)ethenyl)-phenyl)-3-(2-(2-hydroxy-2-propyl)phenyl)thio)methyl)cyclo-propaneacetate. U.S. 5,270,324



C. 1-(((1(R)-(3-(2-(2,3-dichlorothieno[3,2-b]pyridin-5-yl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl)phenyl)-propyl)thio)methyl)cyclopropaneacetic acid or sodium salt thereof. U.S. 5,472,964

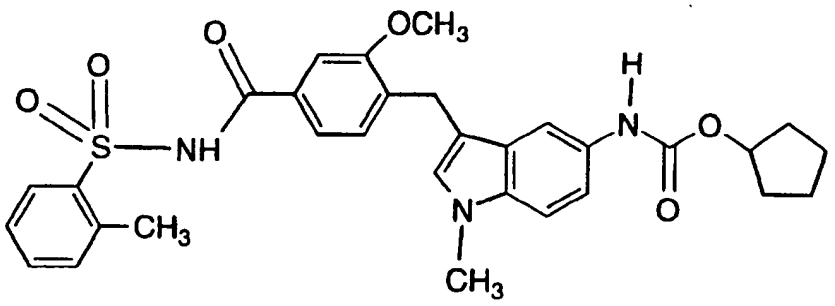


D. N-[4-oxo-2-(1H-tetrazol-5-yl)-4H-1-benzopyran-8-yl]-p-(4-phenylbutoxy)benzamide. EP 173,516



Pranlukast

E. Cyclopentyl-3-[2-methoxy-4-[(o-tolylsulfonyl)carbamoyl]-benzyl]-1-methylindole-5-carbamate. EP 199,543



Zafirlukast

DETAILED DESCRIPTION OF THE INVENTION

The novel pharmaceutical composition of this invention comprises a combination of loratadine and a leukotriene antagonist selected from A, B, C, D and E, described above, as active ingredients, and optionally a pharmaceutically acceptable carrier suitable for enteral or parenteral administration. The formulations may be in solid form, as for example tablets and capsules, or in liquid form, as for example, syrups, elixirs, emulsions and injectables. In the formulation of pharmaceutical dosage forms there generally is utilized excipients such as water, gelatin, lactose starches, magnesium stearate, talc, vegetable oils, benzyl alcohol, gums, polyalkylene glycols, and petroleum jelly. A preferred formulation is mere fully described in the following Example.

In the novel method of treatment of this invention, the loratadine and leukotriene antagonist can be administered substantially concurrently as separate dosage forms or combined in the novel pharmaceutical formulation of this invention.

Although the required dosage will be determined by such factors as the patients age, sex, weight and severity of the condition being treated, the preferred human oral dosage range is about 5 to 20 mg., loratadine, 1 to 3 times per day; preferably about 10 mg. once a day. In the case of the leukotrienes, the human dosage range is also about 5 to 20 mg 1 to 3 times per day; preferably about 10 mg. once a day.

EXAMPLE

Montelukast Sodium 10 mg and Loratadine 10 mg Film Coated Tablet

Amt. Per Tablet	Ingredient
Core	
10.4 mg	Montelukast Sodium
10.0 mg	Loratadine
66.6 mg	Microcrystalline Cellulose, NF
100.0 mg	Lactose Monohydrate, NF
6.0 mg	Croscarmellose Sodium, NF
(60.0 mg)	Purified Water, USP
1.0 mg	Magnesium Stearate, NF
200.0 mg	Core Tablet
Film Coating	
2.25 mg	Hydroxypropyl Methylcellulose 6 cps
1.25 mg	Hydroxypropyl Cellulose LF
1.50 mg	Titanium Dioxide
(33.5) mg	Purified Water
205.0 mg	Film Coated Tablet

WHAT IS CLAIMED IS:

1. A pharmaceutical formulation comprising as active ingredients loratadine and a leukotriene antagonist selected from
(A) montelukast sodium;
(B) Sodium 1-(((R)-(3-(2-(6,7-difluoro-2-quinolinyl) ethenyl)phenyl) -3-(2-(2-hydroxy-2-propyl)phenyl) thio)methylcyclopropaneacetate;
(C) 1-((((1(R)-(3-(2-(2,3-dichlorothieno[3,2-b]pyridin-5-yl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl)phenyl)propyl) thio)methyl)cyclopropaneacetic acid or a sodium salt thereof;
(D) pranlukast; and
(E) zafirlukast;
and a pharmaceutically acceptable carrier.

2. The composition of Claim 1 which is designed for oral administration.

3. The composition of Claim 2 comprising 10 mg of loratadine and 10 mg of a leukotriene antagonist selected from (A), (B), (C), (D) and (E).

4. The composition of Claim 1, wherein the leukotriene antagonist is montelukast sodium.

5. The composition of Claim 4 which is designed for oral administration.

6. The composition of Claim 5, comprising 10 mg of each active ingredient.

7. A method of treating asthma, allergy and inflammation in a patient in need of such treatment by the administration

of an effective amount of loratadine and an effective amount of a leukotriene antagonist selected from:

(A) montelukast sodium;

(B) sodium 1-(((R)-(3-(2-(6,7-difluror-2-quinolinyl)ethenyl)phenyl)-3-(2-(2-hydroxy-2-propyl)phenyl)thio)methyl)cyclopropaneactate;

(C) 1-(((1(R)-(3-(2-(2,3-dichlorothieno[3,2-b]pyridin-5-yl)-(E)-ethenyl)phenyl)-3-(2-(1-hydroxy-1-methylethyl)-phenyl)propyl)thio)methyl)cyclopropaneacetic acid or a sodium salt thereof;

(D) pranlukast; and

(E) zafirlukast;

either substantially concurrently in separate dosage forms or combined in the single pharmaceutical formulation of Claim 1.

8. The method of Claim 7, wherein the pharmaceutical formulation is designed for oral administration.

9. The method of Claim 7 wherein the separate dosage forms and the single pharmaceutical formulation comprise 10 mg of loratadine and 10 mg of a leukotriene antagonist selected from (A), (B), (C), (D) and (E).

10. The method of Claim 7 wherein the leukotriene antagonist is (A) montelukast sodium.

11. The method of Claim 10 wherein the separate dosage forms and single pharmaceutical formulation are designed for oral administration.

12. The method of Claim 11 wherein the separate dosage forms and the single pharmaceutical formulation comprise 10 mg of loratadine and 10 mg of (A), montelukast sodium.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/01799

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 31/41, 31/44, 31/47, 31/405
US CL :514/301, 311, 382, 415

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/301, 311, 382, 415

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,282,233 A (VILANI) 04 August 1981, see column 2, lines 13-19 and column 3, lines 5-12.	1-12
Y	US 4,847,275 A (TODA et al.) 11 July 1989, see column 5, lines 3-6, column 6, lines 58-64, column 90, lines 15-25 and columns 101-102 Example No. 1(230).	1-12
Y	US 5,030,643 A (BERNSTEIN et al.) 09 July 1991, see column 5, lines 55-65 and column 19, lines 45-50.	1-12
Y	US 5,270,324 A (ZAMBONI et al.) 14 December 1993, see column 6, lines 55-60, column 13, lines 10-12, column 68, line 57 - column 69, line 12.	1-12

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents:

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Date of the actual completion of the international search	Date of mailing of the international search report
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/01799

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,472,964 A (YOUNG et al.) 05 December 1995, see column 10, lines 5-14, column 16, lines 3-4, column 67, Example 4B, and column 102, lines 53-61.	1-12
Y,P	US 5,565,473 A (BELLEY et al.) 15 October 1996, see column 8, line 62 - column 9, line 4, column 15 lines 4-6 and column 79, Example 161.	1-12